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Having the right preclinical ocular disease model is a critical factor for your compound’s success. Our scientists have decades of experience with many of the key ocular disease models to help you evaluate your compound’s efficacy in disorders affecting both the front and back of the eye.

Central to the design of these ocular disease models is the rigorous collection and interpretation of objective data. Our experts work with board-certified veterinary and human ophthalmologists and retinal surgeons to ensure capture of optimal data and images. All work is performed on site. Our capabilities include stringent pre-screening ophthalmic exams to eliminate pre-existing ocular defects that could adversely affect the outcome of your ocular studies.
About Absorption Systems
Preclinical Ocular Drug & Device Testing

Services
Small and Large Molecules
Contact Lenses
Devices and Implants
PK Measurements
Bioanalysis
Tolerability
Toxicology
Disease and Efficacy Models
Complete Ocular Exams
Imaging and Diagnostics
Permeability Models
Metabolism Models

Tissues
Lids
LacrimaL Glands
Lacrimal Ducts
Conjunctiva
Sclera
Cornea
Aqueous Humor
Iris
Ciliary Body
Trabecular Meshwork
Lens
Vitreous Humor
Retina
Choroid
Optic Nerve
Adnexa

Equipment
Ophthalmic Surgery Suite
Direct / Indirect Ophthalmoscopy
Slit-Lamp Biomicroscopy
Keratometer
Ultrasound
Optical Coherence Tomography
Fundus Photography
Retinal Photography
Fluorescein Angiography
Auto-Fluorescence
Indocyanine Green (ICG)
Pachymetry
Pneumotonometer for IOPs
ERG, mfERG, VEP
Color Fundus Photography
Corneal Diagnostics
Fluorescein Staining
Schirmer Tear Test

Dose Routes
Topical
Intracorneal
Intravitreal
Intracameral
Periocular
Punctal
Subconjunctival
Subtenon
Subchoroidal
Suprachoroidal
Subretinal

Species
Mouse
Rat
Rabbit
Dog
Pig
Sheep
Allergic Conjunctivitis Model

Study Purpose
Evaluate the efficacy and safety of pharmaceuticals designed to treat allergic conjunctivitis

Deliverables
• Ophthalmic exams using the McDonald-Shadduck scoring system
• Quantitative and qualitative in-life imaging techniques including slit-lamp biomicroscopy and ophthalmoscopy
• Comparison of the test article to currently approved therapeutics
• Tissue excision and histopathological analysis (optional)
• Bioanalysis of analyte concentrations in target tissues (optional)

Model Description
• Animal models are induced by one of the following methods:
  - Parenteral dose of ovalbumin followed by repeated topical dosing of ovalbumin
  - Topical application of compound 48/80
  - Foot pad injection of ragweed pollen followed by repeated topical dosing of ragweed pollen
• Each model is assessed by the McDonald-Shadduck scoring system
• Following induction, subjects may be treated with a test compound and currently marketed therapeutic agent as a positive control

Benefits
• More accurate classification of the test article’s treatment due to treated and untreated control groups
• Consistent scoring of the eyes using FDA-required techniques
• Models are easily reproducible
• Advanced imaging equipment and expertise in-house to perform all evaluations on-site
Corneal Wound Healing Model

**At-a-Glance**

- **Type of model**
  - Evaluation of corneal wound healing drugs and devices

- **Test System**
  - New Zealand White rabbits, Dutch Belted rabbits, pigs, sheep
  - Animals are prescreened for ocular abnormalities

- **Time**
  - 3-5 days post-surgery

**Study Purpose**
Evaluate the efficacy and safety of pharmaceuticals and drug-eluting devices designed to treat corneal epithelial defects

**Deliverables**

- Evaluation of wound healing through clinical ophthalmic examinations using slit lamp biomicroscopy and fluorescein staining
- Digital photographs as necessary to benchmark healing process
- Computer analysis of wound areas to quantitatively measure wound healing
- Comparison of test article to currently approved therapeutics
- Tissue harvest and histopathological analysis (optional)
- Bioanalysis in target tissues (optional)

**Model Description**

- Removal of nictitating membrane (optional)
- Epithelial defect created in the center of the cornea with alcohol
- Epithelium removed using Gill corneal knife or #15 Bard-Parker blade
- Test article implanted by Absorption Systems- or Sponsor-provided surgeon
- Clinical ophthalmic examinations at customized time points
- Positive and negative control groups provide comparative data

**Benefits**

- More accurate classification of the test article’s treatment due to treated and untreated control groups
- Consistent scoring of the eyes using FDA-required techniques
- Advanced imaging equipment and expertise in-house to perform all evaluations on-site
Keratoconjunctivitis Sicca (KCS) Model

Study Purpose
Evaluate the efficacy and safety of pharmaceuticals designed to treat Keratoconjunctivitis Sicca (KCS) or dry eye syndrome

Deliverables
• Evaluation of tear production using Schirmer tear tests and fluorescein tear breakup tests
• Observations of changes in ocular structures throughout the study using slit lamp biomicroscopy and ophthalmoscopy
• Comparison of test article to currently approved therapeutics
• Tissue harvest and histopathological analysis (optional)
• Bioanalysis of analyte concentrations in target tissues (optional)

Model Description
• KCS is induced using atropine and low humidity conditions in New Zealand White rabbits or using a novel ophthalmic airflow chamber in rodents
• Treated control groups are established by administering cyclosporine ophthalmic emulsion in conjunction with atropine
• Ophthalmic exams are performed at customized timepoints to confirm decrease in tear production
• Following induction, subjects may be treated with a test article and currently marketed therapeutic agent as a positive control

Benefits
• More accurate classification of the test article’s treatment due to treated and untreated control groups
• Consistent scoring of the eyes using FDA-required techniques
• Advanced imaging equipment and expertise in-house to perform all evaluations on-site
Anterior Uveitis Model

**At-a-Glance**

**Type of model**
- Induction of uveitis

**Test System**
- New Zealand White or Dutch Belted rabbits
- Animals are prescreened for ocular abnormalities

**Time**
- One week to perform study, plus 4-6 weeks for histopathology

**Study Purpose**
Evaluate the efficacy and safety of pharmaceuticals and drug-eluting devices designed to treat anterior uveitis

**Deliverables**
- Evaluate the ability of test article to treat anterior uveitis
- Comparison of test article to currently approved therapeutics
- Tissue harvest and histopathological analysis
- Ophthalmic exams using the McDonald-Shadduck scoring system

**Model Description**
- Induce uveitis by intraocular injection of lipopolysaccharide (LPS, bacterial endotoxin), Freund’s complete adjuvant, or Mycobacterium butyricum into the anterior chamber of the eye under anesthesia
- Apply test article via topical administration or intracameral injection 24 hours after induction event and after baseline examination
- Perform clinical ophthalmic exams daily for five days after test article administration
- Harvest eyes for histopathological evaluation

**Benefits**
- Animals are pre-screened for ocular abnormalities
- Advanced equipment allows for superior measurements to meet FDA expectations
- Treated and untreated controls allow for better classification of test article efficacy
- Absorption Systems has the equipment and expertise in-house to perform all evaluations on-site

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Glaucoma and IOP-Lowering Drugs Model

Study Purpose
Evaluate the efficacy and safety of pharmaceuticals and drug-eluting devices designed to lower intraocular pressure (IOP) or treat glaucoma.

Deliverables
• IOP measurements at each time point (and pupil size if needed)
• Evaluation of the test article’s ability to reduce intraocular pressure
• Comparison of test article to currently approved therapeutics for the appropriate animal model
• Tissue harvest and histopathological analysis (optional)
• Bioanalysis of analyte concentrations and metabolites in target tissues (optional)

Model Description
• Glaucoma models:
  - Steroid-induction, water provocative test (for short acting drugs), microspheric injection, trabeculectomy, episcleral vein inclusion
• IOP-lowering studies in non-glaucomatous animals
  - Evaluation of glaucoma drugs for lowering IOP from baseline values
• IOP measurements taken at customizable time points with a pneumatometer and other tonometers depending on the species of choice

Benefits
• Animals are pre-screened for ocular abnormalities
• Animals are acclimated to IOP measurement procedures prior to use, ensuring accurate and reliable results
• Acclimated animals can be retained by Customer for use in future studies
• Advanced equipment allows for superior measurements to meet FDA expectations
• Absorption Systems has the equipment and expertise in-house to perform all evaluations on-site

At-a-Glance
Type of model
• Induction of glaucoma

Test System
• New Zealand White or Dutch Belted rabbits, Sprague-Dawley rats, or Beagle dogs
• Animals are prescreened for ocular abnormalities

Time
• 26 days to establish model
• Up to 2 weeks of testing
Diabetic Macular Edema (DME) Model

Study Purpose
Evaluate the efficacy and safety of pharmaceuticals for diabetic macular edema or retinopathy

Deliverables
• Evaluation of the back of the eye at multiple time points via:
  - fundus photography (color)
  - fluorescein angiography
  - optical coherence tomography (OCT)
• Tissue excision and histopathological analysis (optional)
• Bioanalysis of analyte concentrations in target tissues (optional)

Model Description
• Göttingen and Yucatan minipigs possess an area centralis, which is similar to the macula in humans
• A diabetic retinopathy condition in these swine strains will produce small changes in the area centralis that can be utilized as a model for diabetic macular edema
• We use a standard diabetes induction protocol to create this condition

Model Development and Maintenance
• Induce diabetes using standard diabetic induction protocol with streptozotocin
• Monitor health until the animal meets the criteria for classification as diabetic
• Once the model is established, blood glucose levels and selected clinical chemistry parameters will be measured at least three times per week
• All animals are closely monitored by staff veterinarians
• The model can have a duration of up to 18 months

Benefits
• Göttingen & Yucatan minipigs have similar ocular pathophysiology to humans
• Protocol can be customized based on test article-specific treatment and endpoints
• We have the equipment and expertise in-house to perform all evaluations on-site
• Interpretations of pathology performed by a board-certified veterinary pathologist

At-a-Glance

Type of model
• Induction to establish diabetic retinopathy

Test System
• Yucatan or Göttingen minipigs
  • Prescreened for anatomical/physiological abnormalities

Time
• 3-4 weeks to establish model
• Up to 18 months of testing

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Choroidal Neovascularization (CNV) Model

Study Purpose
Evaluate the efficacy and safety of pharmaceuticals designed to treat CNV in rabbits and pigs

Deliverables
• Observations of changes in ocular structures throughout the study using slit lamp biomicroscopy, ophthalmoscopy, color fundus photography, OCT, and fluorescein angiography
• Ability of test article to reduce formation of new blood vessels as well as the number of blood vessels in the eye
• Comparison of test article to currently approved therapeutics
• Tissue harvest and histopathological analysis (optional)
• Bioanalysis of analyte concentrations in target tissues (optional)

Model Description
• CNV and retinal neovascularization are characterized by the creation of new blood vessels in the choroid and retinal layers of the eye and are common symptoms of age-related macular degeneration (AMD)
  - Animals receive subretinal injections of Matrigel™ with bFGF and VEGF
  - Laser photocoagulation may be used for induction
  - Examinations performed at several subsequent customized time points to evaluate presence of neovascularization in retinal and choroidal tissues
  - Following induction, subjects may be treated intravitreally with test articles and currently marketed therapeutic agents as positive controls

Benefits
• Optimal induction of choroidal and retinal neovascularization
• More accurate evaluation due to treated and untreated control groups
• Consistent scoring of the eyes using FDA-required techniques
• Advanced equipment and expertise in-house to perform all evaluations on-site
Ocular PK and Distribution Studies

At-a-Glance

Type of model
• Ocular PK and distribution

Test System
• New Zealand White or Dutch Belted rabbits, rodents, pigs, non-human primates, dogs, sheep
• Animals are prescreened for ocular abnormalities

Time
• 2-3 weeks

Study Purpose
Evaluate the ocular distribution of pharmaceuticals in various species

Deliverables
• Concentration of test compound in each tissue
• Pharmacokinetics profile determination (optional)

Model Description
• Dose routes: corneal, intracameral, intravitreal, periocular, punctal, subconjunctival, subtenon

• Tissue Collection:
  lids, conjunctiva (bulbar and palpebral), cornea, aqueous humor, iris, ciliary body, lens, trabecular meshwork, vitreous humor, choroid, retina, sclera, optic nerve, lacrimal glands
  Vitreous humor, choroid, ciliary body, and retina can be sectioned for further quantification based on area of these tissues
  LC-MS/MS analysis of collected tissues in matched or representative tissue matrix
  LC-MS/MS analysis of blood and PK analysis using WinNonlin® (optional)

Benefits
• Pre-screening ophthalmic examinations on all animals prior to study start to eliminate ocular abnormalities
• Integrated formulation and bioanalytical services
• Standard PK processes to ensure no contamination and consistent collection of the right tissues
• Dedicated operations manager to facilitate study conduct and minimize turnaround time

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Contact Lens Studies

Study Purpose
Evaluate the placement and retention of contact lenses in various species

Deliverables
• Placement, removal, and retention time for each contact lens
• Observations and test scores for each examination

Model Description
• Pre- and post-study clinical ophthalmic examination including ophthalmoscopy, slit-lamp biomicroscopy, fluorescein staining, and McDonald-Shadduck scoring system
• Contact lenses evaluated at multiple customized time points for gross observations, retention, lens centration, edge lift, primary gaze movement, lens tightness, and/or fit evaluation
• Histopathology (optional)

Benefits
• Pre-screening ophthalmic examinations and contact lens conditioning for all animals prior to study start
• Dedicated operations manager to facilitate study conduct and minimize turnaround time
• Standard protocols for lens application and removal
• Consistent scoring of the eyes using FDA-required techniques
• Bioanalytical capabilities for combined pharmacokinetic (PK) studies
Ocular Device Studies

At-a-Glance

Type of model
• Evaluation of intraocular drug-eluting devices

Test System
• New Zealand White or Dutch Belted rabbits
• Pigs or minipigs
• Sheep or goats

Time
• Up to 6 months

Study Purpose
Evaluate the efficacy, safety, and potency of drug-eluting intraocular devices

Deliverables
• Placement and efficiency of device
• Observations and test scores for each examination

Model Description
• Pre- and post-study clinical ophthalmic examination including indirect ophthalmoscopy, slit-lamp biomicroscopy, fluorescein staining, and McDonald-Shadduck scoring system
• Schirmer tear tests, corneal staining, ultra-sound imaging and intraocular pressure measurements (use of pneumatonometer), pachymetry as needed
• Routine animal observations
• Efficacy evaluation in animals with induced disease (optional)
• Histopathology (optional)
• Bioanalysis/ Biomarker analysis (optional)
• Imaging diagnostics (e.g. OCT, ERG, fluorescein angiography)

Benefits
• Dedicated operations manager to facilitate study conduct and minimize turnaround time
• Consistent scoring of the eyes using FDA-required techniques
• On-site scientists with professional experience with small and large animals
• Bioanalytical capabilities for combined pharmacokinetic (PK) studies
• Consultative assistance in animal model selection
• Access to board certified veterinary ophthalmologists
• State-of-the-art diagnostic equipment
Intraocular Lens (IOL) Studies

Study Purpose
Evaluate the Sponsor’s intraocular lens implant in vivo

Deliverables
• Surgeon and/or specialized equipment to perform surgeries
• Animal prescreening and post-operative care
• Surgical procedures recorded and provided on DVD
• Clinical ophthalmic exams scored using McDonald-Shadduck scoring system and/or Sellman and Lindstrom fibrosis scoring of posterior capsule opacification (PCO)

Model Description
• Animal anesthetized and prepared for surgery
• Natural lens removed via phacofragmentation
• Sponsor IOL implanted by Sponsor surgeon or Absorption Systems ophthalmologist
• Surgical eye is maintained with BSS and viscoelastic during surgery
• Follow-up exams include clinical ophthalmic exams and post-operative treatment
• Imaging including photo slit lamp, anterior OCT, and/or specular microscopy

Benefits
• State-of-the-art surgical suite with specialized equipment and supplies
• Access to human and veterinary ophthalmologists to perform custom procedures
• Standardized protocols for pre- and post-operative animal care

At-a-Glance

Type of model
• Evaluation of intraocular lenses

Test System
• Rabbits
• Dogs
• Minipigs
• Animals are prescreened for ocular abnormalities

Time
• 2-4 weeks
Other Models

When selecting an appropriate animal model for predicting efficacy of a drug, it is important to match the etiology of the disease state as closely as possible to the human condition. However, for most ocular diseases, there is no standard, predefined preclinical testing model. The species, method of induction, and deliverables must be customized based on the test article characteristics and desired study endpoints (i.e. distribution, safety, and/or efficacy). Studies intended for regulatory submission should be discussed with the regulatory body beforehand to confirm the appropriate design and animal model has been selected. Our experienced scientists will guide you through the pros and cons of each model to maximize study outcomes while observing the 3R’s of animal research (Replacement, Refinement, and Reduction). Custom models we are developing include:

**Photopic Retinal Damage in Mouse**
- Light induced retinopathy
- Baseline and post light damage ERG readings

**Corneal Graft in Rabbit**
- Corneal transplant
- Ophthalmic exams, endothelial cell count, photo slit lamp, anterior chamber OCT, and histopathology

**Cataract Model in Rabbit**
- Cataract induction
- Qualitative and quantitative assessment of cataracts after treatment with test article

**Infectious Conjunctivitis in Rabbit**
- Inoculation by an appropriate bacterial strain
- Ophthalmic exams, including anterior chamber OCT and photo slit lamp, to compare test article treatment to a marketed product
About Absorption Systems

Absorption Systems assists pharmaceutical and medical device companies in identifying and overcoming ADMET (Absorption, Distribution, Metabolism, Excretion, and Toxicity) barriers in the development of drugs and medical devices. The company’s mission is to continually develop innovative research tools that can be used to accurately predict human outcomes or to explain unanticipated human outcomes when they occur. The company’s facilities are strategically located on both US coasts and Panama, and encompass nearly 65,000 sq. ft., servicing hundreds of customers throughout the world. You can trust results based on our senior scientists and support staff’s experience with GLP-compliant processes and international regulatory standards, as well as our AAALAC-accredited and NIH-assured facility. For more information on the company’s comprehensive contract services and applied research programs, please visit absorption.com.

Preclinical Services & Capabilities

Lead Optimization
Physicochemical Properties
Permeability
Stability
Metabolism and Transporters
Binding and Distribution
Formulation Assessment
Bioavailability and Exposure | rodent, non-rodent

Candidate Selection
Formulation Development
PK and Biodistribution | multiple species and dose routes
Barriers to Bioavailability
In Situ and Isolated Organ Perfusion | rat: brain, liver, intestine
Ex Vivo Tissue Permeability | intestinal, dermal, ocular, buccal, nasal, vaginal

IND- and NDA-Enabling
Transporter-Based Drug Interactions
BCS Permeability and Solubility
Classification for Bio waivers
Metabolism-Based Drug Interactions
Metabolite ID and Production
Medical Device Testing
Toxicology

Bioanalysis
Bioanalytical Support from Discovery through Clinical
GLP and Non-GLP